

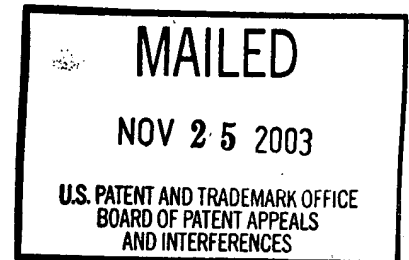
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte HARRIET L. ROBINSON, ELLEN F. FYNAN,
ROBERT G. WEBSTER, and SHAN LU

Appeal No. 2001-2316
Application No. 08/187,879

ON BRIEF¹



Before WILLIAM F. SMITH, ADAMS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the
examiner's final rejection of claims 44-46, 50, 51 and 81-89. The examiner
indicated that the only other claims pending in this application, claims 62-64, 68-
70, 74, and 78-80, were allowable. Answer, page 2.

¹ Appellants waived their request for oral hearing. Paper No. 52. Accordingly, we considered this
appeal on Brief.

Claim 44 is illustrative of the subject matter on appeal and is reproduced below:

44. A method of immunizing a mammal against an immunodeficiency virus of interest selected from the group consisting of: simian immunodeficiency virus and human immunodeficiency virus, said method comprising administering to the mammal a DNA transcription unit comprising DNA encoding an antigen of said immunodeficiency virus of interest operatively linked to DNA which is a promoter region, in a physiologically acceptable carrier, wherein the DNA transcription unit is expressed in cells of the vertebrate, whereby the mammal is protected from disease caused by said immunodeficiency virus of interest.

The references relied upon by the examiner are:

Rekosh et al. (Rekosh), "Coexpression of human immunodeficiency virus envelope proteins and tat from a single simian virus 40 late replacement vector," Proc. Natl. Acad. Sci., Vol. 85, pp. 334-338 (1988)

Hoffenback et al. (Hoffenback), "Unusually high frequencies of HIV-specific cytotoxic T lymphocytes in humans," J. Immunology, Vol. 142, pp. 452-462 (1989)

Johnson et al. (Johnson), "SIV Infection of Macaques as a Model for AIDS Pathogenesis," Intern. Rev. Immunol., Vol. 8, pp. 55-63 (1992)

(Kuby), Immunology p. 477 (Janis Kuby, ed., W.H. Freeman and Co., New York) (1992)

Tang et al. (Tang), "Genetic immunization is a simple method for eliciting an immune response," Nature, Vol. 356, pp. 152-154 (1992)

Haynes, "Scientific and social issues of human immunodeficiency virus vaccine development," Science, Vol. 260, pp. 1279-1286 (1993)

Butini et al. (Butini), "Comparative analysis of HIV-specific CTL activity in lymphoid tissue and peripheral blood," J. Cellular Biochem., Suppl. 18B:147 Abst. No. J306 (1994)

Gilboa et al. (Gilboa), "Gene therapy for infectious diseases: the AIDS model," TIG, Vol. 10, No. 4, pp. 139-144 (1994)

Glaser, "Biotech firms shift focus toward therapeutic HIV vaccine development," Genetic Engineering News, p. 6 (January 1, 1996)

Weiss, "Genetic vaccine keeps chimps protected against AIDS virus," The Washington Post, p. A2 (April 30, 1997)

Cohen et al. (Cohen), "HIV/AIDS in 1998 – gaining the upper hand?," JAMA, Vol. 280, No. 1, pp. 87-88 (1998)

GROUND OF REJECTION

Claims 44-46, 50, 51 and 81-89 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the full scope of the claimed invention.

We affirm.

CLAIM GROUPING

According to appellants (Brief, page 4), claims 44-46, 50, 51 and 81-89 stand or fall together. Accordingly, we limit our discussion to representative independent claim 44. Claims 45, 46, 50, 51 and 81-89 will stand or fall together with claim 44. 37 CFR § 1.192(c)(7).

DISCUSSION

According to the examiner (Answer, page 8), appellants' specification is enabling only for claims directed to:

- (I) A method of reducing SIV [simian immunodeficiency virus] infected cells in a mammal², the method comprising

² In the event of further prosecution, we encourage the examiner to reconsider the record to determine if, in fact, the evidence of record will support a claim to a method of reducing SIV or HIV infected cells in a mammal. As we understand the record, the evidence demonstrates a reduction in "viral loads," not "infected cells." See, Robinson Declaration, page 3, "viral loads were reduced to the chronic level over a shorter period of time in the vaccinated animals..., than the control animals." If, on reflection, the examiner finds that the evidence is directed to reducing viral loads and not infected cells, we encourage the examiner to clarify the record as to whether such a method would meet the statutory requirements of 35 U.S.C. § 101. See e.g., Brief, page 8, wherein appellants argue, "a method of reducing viral load clearly presents a substantial utility."

administering to said mammal multiple administrations of a mixture of DNA plasmid vectors: pSIV239.dpol, SIV239.sgp130, SIV251.sgp130, SIV316.sgp130 and SIV239.sgp110, in a physiologically acceptable carrier, wherein said multiple administrations comprise at least a gene gun administration of one of the DNA plasmid vectors to the skin of the mammal, whereby the SIV infected cells are reduced in the mammal as a result of SIV antigen expression by the administered plasmid vectors; and

- (II) A method of reducing HIV [human immunodeficiency virus] infected cells in a mammal, the method comprising administering to said mammal multiple administrations of a mixture of DNA plasmid vectors: pCMV/HIV-1-NL4-3.dpol, pCMV/HIV-1-HXB-2.env, pCMV/HIV-NL4-3env, Jw4303/HIV-1-HXB-2.sgp120, and JW4303/HIV-1-HXB-2.sgp140, in a physiologically acceptable carrier, wherein said multiple administrations comprise at least a gene gun administration of one of said DNA plasmid vectors to the skin of said mammal, whereby the HIV infected cells are reduced in the mammal as a result of HIV antigen expression by the administered plasmid vectors.

As the examiner explains (Answer, page 9), given its broadest reasonable interpretation, claim 44 encompasses a method of immunizing any mammal, including humans, against SIV or HIV by administering any DNA encoding any SIV or HIV antigen so as to generate a "complete" protective response against an infection of any SIV or HIV strain. In support of the examiner's construction of claim 44 we note that appellants define the term "immunizing" in the context of the protective response sought. For example, at page 7 of the specification, appellants disclose, "[t]he term "immunizing" refers herein to the production of an immune response in a vertebrate which protects (... totally) from the manifestations of infection (i.e., disease) caused by an infectious agent. That is,

a vertebrate immunized by the present invention will not be infected..." by SIV or HIV.

35 U.S.C. § 112, first paragraph requires appellants' specification to contain a written description of the claimed invention and the manner and process of making and using that invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to which that invention pertains, or with which it is most nearly connected, to make and use that invention. Although not explicitly stated in the first paragraph of 35 U.S.C. § 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371-72, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999); In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); In re Wands, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

When rejecting a claim under the enablement requirement of 35 U.S.C. § 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. If the examiner meets this burden, the burden then shifts to appellants to provide suitable proofs indicating that the specification is indeed enabling. In re Marzocchi, 439 F.2d 220, 223-224, 169 USPQ 367, 369-70

(CCPA 1971). To assist the examiner in meeting his initial burden of setting forth a reasonable explanation as to why he believes the scope of the claimed invention is not adequately enabled by the description, our appellate reviewing court has outlined a number of factors to consider. As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the nature of the invention, the breadth of the claims, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the quantity of experimentation necessary, the amount of direction or guidance presented, and the presence or absence of working examples.

On this record, the examiner has addressed these factors and found that they weight in favor of nonenablement. For the reasons discussed below, we agree.

I. The nature of the invention:

As appellants disclose (specification, page 2), “[t]he present invention relates to the use of DNA transcription units for raising immune responses.” In addition, appellants disclose (specification, page 3), “DNA transcription units introduced by the present method can be used to express any antigen encoded by an infectious agent, such as a virus, ... as well as antigenic fragments and peptides that have been experimentally determined to be effective in immunizing an individual against infection by a pathogenic agent.”

II. The breadth of the claims:

As discussed, supra, the claims are very broad. As the examiner explains (Answer, page 9), the scope of claim 44 encompasses a method of immunizing any mammal, including humans, against SIV or HIV by administering any DNA encoding any SIV or HIV antigen so as to generate a "complete" protective response against an infection of any SIV or HIV strain. Appellants' characterization (see e.g., Reply Brief, page 4) of the claimed invention is consistent with that of the examiner's. Furthermore, appellants emphasize (Reply Brief, page 4), the specification's definition of the term "immunizing," arguing, "'immunizing' does not refer solely to protection against infection per se ... but rather, refers also to generation of an immune response that lessens or eliminates manifestations of disease after infection with the infectious agent." While the examiner acknowledges that appellants' characterization of the claimed invention is correct, the examiner finds (Supplemental Answer, bridging paragraph, pages 3-4), "the breadth of the DNA immunization methods against any SIV or HIV infection is not commensurate with the scope of enablement provided by the specification at the time [the] invention was made (1992)."

III. The state of the prior art:

According to the examiner (Supplemental Answer, bridging paragraph, pages 5-6)

"on the basis of the evidentiary support disclosed in the prior art of record, DNA immunization against a naturally occurring HIV or SIV infection in a mammal (primates such as monkeys and humans) in 1992-1/1994 is not an established but rather an emerging

technology that was still undergoing research for an art-recognized model and/or efficacy of any protection....

In support of this finding, the examiner relies on Hayes, Hoffenbach, Butini, Glasser, Rekosh, Weiss, Cohen, Kuby, Gilboa and Johnson.

Appellants, however, point out (Reply Brief, page 10) that Hoffenback and Butini "cited by the [e]xaminer describe investigation of HIV-specific CTL activity in humans infected with the HIV virus." In this regard, appellants argue (id.), that they "are not claiming a specific CTL or antibody response; rather, the claims are drawn to immunization and protection against manifestations of infection...."

According to appellants (id.), "what is required by the claimed invention is not that a particular mechanism or type of immune response be generated, but rather, that the immune response which is generated by the DNA vaccine, protects ... from the manifestations of infection (i.e., disease) caused by the infectious agent." With regard to Glaser, appellants argue (Reply Brief, page 11):

even if latent HIV were to reside in immunoprivileged sites following infection, partial protection (e.g., immunization that causes a rapid reduction in viral load, such as that described in the Data Declaration) would still be possible, thus allowing generation of an immune response that lessens manifestation of disease and demonstrating "immunizing" as the term is described in the Specification.

While appellants' argue that it would be possible to generate an immune response that lessens manifestation of disease, the full scope of the claimed invention (see claim 44) requires that "the mammal is protected from disease caused by said immunodeficiency virus of interest." Read in light of the

specification (e.g. page 7, emphasis added), "a vertebrate immunized by the present invention will not be infected or will be infected to a lesser extent than would occur without immunization." See also, Reply Brief, page 4, "'immunizing' does not refer solely to protection against infection per se (although that is contemplated)...." Thus, lessening the manifestation of disease is merely one component of the full scope of the invention claimed.

Appellants' recognize (Reply Brief, page 11), the examiner's reference to Rekosh, Weiss and Cohen acknowledging that these references "point out the difficulties associated with development of a vaccine targeting HIV." Nevertheless, appellants argue (id., emphasis added) that they have "demonstrated that immunization of a mammal by administering to the mammal a DNA transcription unit comprising a DNA encoding an antigen of SIV, whereby the mammal was protected at least partially from the manifestations of disease caused by the SIV, is indeed possible." As discussed above, partial protection is merely one component of the full scope of appellants' claimed invention. What is missing is evidence demonstrating that the specification provides an enabling description of the full scope of the claimed invention..

IV. The relative skill of those in the art:

While neither the examiner nor appellants take issue with the level of skill in the art, we find the level of skill in the art of genetic engineering and immunology to be high. Cf. Enzo, 188 F.3d at 1373, 52 USPQ2d at 1137; Wands, 858 F.2d at 740, 8 USPQ2d at 1406.

V. The amount of direction or guidance presented/ the presence or absence of working examples:

According to the examiner (Answer, page 10), "examples 11-15 of the specification describe making and administering DNA vectors encoding antigens of SIV and HIV, but [a]ppellants have not provided any guidance and/or factual evidence showing a reasonable extrapolation from the disclosure any DNA vaccine/immunization or protective effect." In this regard, we note that example 14 of appellants' specification is prophetic in nature and does provide any evidence supporting appellants' claimed invention. Instead, according to appellants (Brief, page 5), example 14 simply "sets forth how to conduct a vaccine trial to assess efficacy of the constructs." In our opinion, the Robinson declaration also does not support the full scope of appellants' claimed invention. According to the Robinson declaration (§ 3), "[t]he protocol for the trial is similar to that described in the [s]pecification at [e]xample 14." However, Robinson declares (§ 5, emphasis added), "[t]he DNA immunizations did not prevent infection or protect against CD4+ cell loss. ... Notably, however, viral loads were reduced to the chronic level over a shorter period of time in the vaccinated animals..., than in the control animals."

At best, the Robinson declaration, when viewed in light of appellants' specification, provides evidence that the claimed invention is capable of reducing viral loads. However, in our opinion, demonstrating that viral loads can be reduced is not sufficient to enable the entire scope of appellants' claimed invention which encompasses a method of immunizing any mammal, including

humans, against SIV or HIV by administering any DNA encoding any SIV or HIV antigen so as to generate a "complete" protective response against an infection of any SIV or HIV strain. As the examiner explains (Answer, bridging sentence, pages 10-11):

neither the application, nor any of the Declaration[s] of record, nor any prior art of record, nor any art of record even five years after the effective filing date of the application shows by factual evidence that any administration of any SIV or HIV antigen expressing plasmid vector as disclosed by the as-filed specification by any delivery route so as to generate a protective response against SIV and/or HIV can be reasonably reproduced in a representative number of SIV or HIV infectious mammals including humans.

VI. The predictability or unpredictability of the art/ the quantity of experimentation necessary:

To demonstrate the unpredictability of the art at the time the invention was made the examiner relies on Haynes (Answer, bridging paragraph, pages 14-15), to teach

immune correlates for protection against HIV are not known, that there is no animal model that mirrors human HIV infection, and that current animal models for HIV infection do not develop AIDS symptoms or anti-HIV immune responses analogous to those of HIV-infected humans, so that it is impossible to determine whether observation of a given immune response to an immunodeficiency virus vaccine in an animal model indicates that any HIV antigen expressing DNA vaccine plasmid vector would actually confer any protection against HIV infection in any infectious mammal including humans....

In addition, the examiner notes that similar to the claims on appeal here, the claims in In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993), encompassed "vaccines against AIDS viruses and that, because of the

high degree of genetic, antigenic variations in such viruses, no one has yet ... developed a generally successful AIDS virus vaccine.”

In response to the examiner’s findings, appellants rely on Gardner³ and McClure⁴, arguing (Reply Brief, page 8), “SIV-infected nonhuman primates are an excellent animal model system for studies which include studies of vaccines.” Appellants, however, fail to point out with any particularity how these references provide evidence that a skilled artisan, at the time the instant application was filed, would have been able to carry out, without undue experimentation, the full scope of the claimed method. For example, appellants fail to explain how these references relate to the issue of antigenic variability.

We note that appellants agree (Reply Brief, page 11) that the references cited by the examiner “emphasize problems relating to genetic variability of HIV antigens and its impact on development of an AIDS vaccine....” However, appellants argue (id., emphasis added) that the references emphasize the importance of appellants’ invention, because “[a]ppellants have ... demonstrated that immunization of a mammal by administering to the mammal a DNA transcription unit comprising a DNA encoding an antigen of SIV, whereby the mammal was protected at least partially from the manifestations of disease caused by the SIV, is indeed possible.” In our opinion, however, appellants’ arguments serve to emphasize that the specification does not support the full

³ Gardner, *Dev. Biol. Stand.*, Vol. 72, pp. 259-66 (1990). We were unable to locate a copy of this reference in the administrative file.

⁴ McClure, *Ann. NY Acad. Sci.*, Vol. 616, pp. 287-98 (1990). We were unable to locate a copy of this reference in the administrative file.

scope of the claimed invention, which encompasses a "complete" protective response against an infection of any SIV or HIV strain.

It is our opinion, that the examiner has set forth a reasonable basis for finding that the scope of the appealed claims is not enabled by the general description and prophetic example (example 14) in the specification.

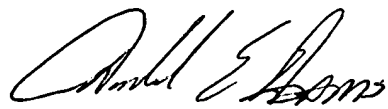
Consequently, the burden of proof was properly shifted to appellants to present persuasive arguments, supported by suitable proofs where necessary, that appellants' specification provides an enabling description for the full scope of appellants' claimed invention. As discussed, supra, the Robinson declaration fails to demonstrate a complete protective response. We are also not persuaded by appellants' rhetorical arguments (Brief, pages 7-8), regarding the virulence and quantity of challenge virus used. These arguments are not supported by evidence on this record. Accordingly, it is our opinion that appellants failed to meet their burden of proof.

On reflection, it is our opinion that the majority of the Wands factors weigh in favor of nonenablement. Accordingly, we affirm the rejection of claim 44 under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the full scope of the claimed invention. As set forth, supra, claims 45, 46, 50, 51 and 81-89 fall together with claim 44.

No time period for taking any subsequent action in connection with this
appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Lora M. Green
Administrative Patent Judge

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Appeal No. 2001-2316
Application No. 08/187,879

Page 15

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